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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/634,970 | 08/05/2003 | J. Milton Harris | SHE0010.13 | 6943 |
| 21968 | 7590 | 02/22/2006 | EXAMINER | |
| NEKTAR THERAPEUTICS 150 INDUSTRIAL ROAD SAN CARLOS, CA 94070 | | | NAFF, DAVID M | |
| | | | ART UNIT | PAPER NUMBER |
| | | | 1651 | |
| DATE MAILED: 02/22/2006 | | | | |

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/634,970

Applicant(s)

HARRIS ET AL.

Examiner

David M. Naff

Art Unit

1651

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 December 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 68-96 is/are pending in the application.
- 4a) Of the above claim(s) 68-77 and 95 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 78-94 and 96 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 05 August 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 11/15/04.
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: _____.

DETAILED ACTION

Claims in the application are 68-96.

A response of 12/7/05 to a restriction requirement of 11/10/05 elected Group II claims 78-94 and 96 with traverse.

5 The traverse is on the ground that search of potential art is simultaneously useful for each of the two groups, and a serious burden will not result from searching and examining all the claims. However, due to the difference in the method of Group I from the method of Group II as stated in the restriction requirement, different searches
10 and different consideration in regard to prior art will be required that will be a serious burden. The restriction requirement is still considered proper, and is adhered to and made final.

Claims 68-77 and 95 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention,
15 there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 12/7/05.

Claims examined on the merits are 78-94 and 96.

The Kitaguchi et al document listed on page 3 of the 1449 of
20 11/15/04 has been lined through since a copy was not received in a parent application.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C.

112:

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5 The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

 Claims 78-94 and 96 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not
10 described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

 Support is not found in the specification for an invention required by claims 78-94 and 96, which are new claims that replaced
15 original claims. The specification fails to disclose that the invention is a method of preparing a purified polymer as required by claims 78-94 and 96. According to the specification (11, line 15 to page 17, line 28) the invention provides a multi-armed polymer derivative having a structure as set forth on page 12 or 15. It is
20 also stated (page 16, beginning at line 3) that the invention includes methods of synthesizing the polymers. There is found no disclosure that the invention is to include a method of purifying a polymer, and none of the original claims required such a method. While purifying is disclosed after synthesizing the polymer, this is disclosed only in
25 regard to purifying a polymer having a specific structure using ion exchange chromatography where specific polymeric materials are removed. The specific methods of purifying described do not support extrapolating to the broader scope of a method of purifying presently

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claimed that encompasses purifying any polyethylene glycol (PEG) polymer having an end capping group and site suitable for interacting with ion exchange chromatography media to remove one or more polymeric impurities selected from the group consisting of PEG diol, end capped PEG-OH and activated end-capped PEG. This concept of a method of purification being the invention is not disclosed or supported in the specification, or any of the original claims. Furthermore, the specification does not describe or support modifications of the method of claim 78 as required by dependent claims 79-94 and 96. The portions of the specification referred to in the preliminary amendment of 8/5/03 as providing support have been noted. However, these portions relate to purifying a specific polymer by a specific method and removing specific polymers that are impurities. This does not support a purification method of broader scope as presently claimed that presents a different concept of the invention than described by the portions of the specification cited in the preliminary amendment.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C.

112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 78-94 and 96 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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The claims are confusing and unclear as to polymer structures required by claim 78 by reciting a "PEG polymer comprises an end capping group and site suitable for interacting with ion exchange chromatography media", "PEG diol", "end capped PEG-OH" and "activated end-dapped PEG". The specification does not describe metes and bounds of the polymers as claimed. The disclosure of specific polymers within the scope of the polymers recited does not define the broader language of the claims.

Claim Rejections - 35 USC § 103

10 The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

15 (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

20 This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

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Claims 78-94 and 96 are rejected under 35 U.S.C. 103(a) as being unpatentable over Martinez et al (5,643,575) in view of Yoakum (4,650,909) and El-Tayar et al (6,638,500 B1), and if necessary in further view of Sartore et al (listed on 1449), Veronese et al (pp 5 127-137) (listed on 1449), Abuchowski et al (listed on 1449) or Seely (5,935,564).

The claims are drawn to method for preparing a purified polymer by providing an impure polymer composition comprising a PEG polymer having an end capping group and site suitable for interacting with ion 10 exchange chromatography media, and one or more polymeric impurities selected from the group consisting of PEG diol, end capped PEG-OH and activated end-capped, and purifying the impure polymer composition by ion exchange chromatography to provide the PEG polymer in substantially pure form.

15 Martinez et al disclose branched polymers that provide extended *in vivo* circulating life of biologically active materials (col 1, lines 6-9). The polymer can be lysine disubstituted with MPEG (last formula of claim 39) that has the same structure as the polymer presently claimed. The MPEG disubstituted lysine is purified by 20 conventional methods (col 7, lines 12-15), and after conjugating to a biologically active nucleophile such as a blood factor (col 7, line 37) is purified such as by diafiltration or column chromatography (col 9, lines 27-30).

Yoakum discloses removing toxic aldehydes and ketones (col 2, 25 lines 53-59) from polyethylene (PEG) using ion exchange resins

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(paragraph bridging cols 3 and 4) so the PEG can be used for transfection of human cells.

El-Tayar et al disclose using ion exchange chromatography (col 7, lines 5-6) to purify a PEG-polypeptide conjugate.

5 Sartore et al disclose modifying arginase with monomethoxy polyethylene glycol (MPEG), and purifying the modified arginase from excess reagents and by-products of the reaction using column chromatography (page 48, last three lines of the paragraph under "Arginase Modifications").

10 Veronese et al disclose enzyme modification with MPEG. Unreacted MPEG-OH is removed from the modified enzyme by gel filtration in the final step of purification (page 129, last sentence of the 4th complete paragraph).

Abuchowski et al disclose attachment of PEG to asparaginases.
15 Unbound SS-PEG is removed by dialysis using an Amicon DC-2 hollow fiber device equipped with an H1P100 cartridge (paragraph bridging pages 176 and 177).

Seely discloses (col 3, lines 13-22) purifying PEGs using hydrophobic interaction chromatography (HIC) to separate the PEGs
20 based on their size and their in-group functionality. The purified PEGs can be used to modify biologically active molecules.

It would have been obvious to use ion exchange chromatography to purify the MPEG disubstituted lysine of Martinez et al as suggested by Yoakum using ion exchange resins to purify PEG and El-Tayar et al
25 using ion exchange chromatography in purifying a PEG-polypeptide

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conjugate since Martinez et al suggest using conventional purifying methods. Preparing the MPEG disubstituted lysine of Martinez et al would have inherently resulted in a polymeric impurity as required by the present claims. The COOH group of the MPEG disubstituted lysine of Martinez et al (claims 39) is capable of interacting with an ion exchange resin. The disclosure of purifying a PEG-modified protein by Sartore et al, Veronese et al or Abuchowski et al, or purifying PEGs by separating PEGs having different molecular weights or end-groups by Seely, if needed, would have further suggested conditions for purifying the MPEG disubstituted lysine of Martinez et al. The Seely patent is a reference even through it has an effective filing date of 3/6/96 since the presently claimed invention is not described in the parent applications. The conditions of dependent claims would have been matters of obvious choice in view of conditions disclosed by the references. The parent applications do not antedate Seely and El-Tayar et al since the presently claimed invention is not disclosed in the parent applications.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*,

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686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

5 A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

10 Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 78-94 and 96 are rejected on the ground of nonstatutory
15 obviousness-type double patenting as being unpatentable over claims 1-49 of U.S. Patent No. 5,932,462. Although the conflicting claims are not identical, they are not patentably distinct from each other because the presently claimed method of purifying a PEG polymer would have been suggested by the method of purifying a PEG polymer by ion
20 exchange chromatography suggested by the patent claims.

Double Patenting

Claims 78-94 and 96 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 96-109, 111, 112 and 114-133 of copending Application No.
25 10/119,546. Although the conflicting claims are not identical, they are not patentably distinct from each other because the presently claimed method of purifying a PEG polymer would have been obvious from the method of purifying a PEG polymer of claims of the co-pending application.

30 This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

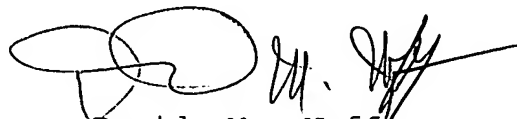
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Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David M. Naff whose telephone number is 571-272-0920. The examiner can normally be
5 reached on Monday-Friday 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

10 Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For
15 more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


David M. Naff
Primary Examiner
Art Unit 1651

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DMN
2/17/06